

## *Gymnema sylvestre*: An Herbal Hope of Diabetes Care and Management

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### Abstract

Medicinal plants served as a platform for ancient Ayurvedic system of medicine. In the present scenario, herbal therapeutics is gaining momentum in pharmacological applications and as molecular targets in the drug development. The emerging trend in rising incidence of diseases and associated complications with commercial medications poses a serious threat to mankind. Naturopathic treatments offer respite from the high cost of expensive drugs as well as in being comparatively safe with less side effects. It is estimated that nearly 80% of population depends on the natural remedies for health care.

Plants are a valuable source of a number of bioactive compounds like alkaloids, quinine, paclitaxel, opium alkaloids, quinine, atropine, and cardiac glycosides (digitalis, obtain) to name a few. The first anti-diabetic drug, metformin, isolated from *Galega officinalis*, was an herbal formulation. Thus, it becomes very important to screen plants with pharmacological significance as a basis for the development of newer and more effective therapeutics. Therefore, we are here in presenting the physicochemical and pharmacological properties of the *Gymnema sylvestre* as an adjunctive treatment to those who are established diabetics in which doses of the allopathic hypoglycemic get reduced so as to their complications and side-effects; and secondly as an alternative to those who are in prediabetic range and can control their blood sugar levels with exercise, diet control and use of these herbal remedies which are obviously less harmful.

**Keywords:** Diabetes; Herbal drugs; Plant medicine; *Gymnema sylvestre*; Anti-diabetic agents; Ayurveda; Mesasrngi; Hyperglycemia; Gurmar

**Abbreviations:** NIDDM: Non-insulin dependent diabetes mellitus; ATP: Adenosine triphosphate

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### Introduction

The herbal treatment for many diseases has been investigated throughout the world since long time as no wonder these herbal medicines were effectively used by the local natives to treat their ailments. Therefore, these herbs, plants, trees and many other floras have been the target for research by the scientist to explore new drugs or formulations to treat various diseases by taking crude references

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through the local natives. Ayurveda, an established Indian system of medicine is full of these references in terms of extensive use of plants, herbs, herb mineral compounds in management of various diseases. Indian flora have been investigated extensively worldwide and found that many of them have great pharmacological significance.

Diabetes mellitus is a major endocrine disorder affecting nearly 10% of the population worldwide and a key issue of concern. The disease is a syndrome which virtually affects all parts of the human body leading to simple ailments to multi-organ complications [1, 2]. Diabetes mellitus is a disorder of carbohydrate, fat, and protein metabolism, characterized by chronic hyperglycemia and the development of chronic, severe complications. At present, it is estimated that 150 million people across the globe have diabetes with the number expected to increase to 366 million by the year 2030 [3-5]. Given this rise in the prevalence of diabetes, the myriad associated complications, and the shortfalls of existing treatment options, more effective interventions need to be sought. Though the very effective use of oral hypoglycemic drugs have been experienced since long, the treatment of type-2 diabetes is still posing a major problem due to therapy failure. Such failure is evident in a majority of patients after 10 years treatment with sulfonylureas, which stimulate insulin release by closure of B-cell K-ATP channel probably due to development of tolerance [6,7].

Though there are fair good prospects of herbal medicines, very little scientific validation restricts the wide use of all these products. These products need wide and extensive research work to elucidate important active principles to be used as drug. Very few have been experimentally validated and scientifically approved as medications for the treatment of various diseases [8]. Herbal treatment for diabetes mellitus is well-known and thus may be able to lead to compounds with such a combination of ideal therapeutic properties. According to an earlier review of herbs and nutrient supplements that were claimed to improve glycemic control few plants were supported by rigorous clinical evidence. The herbs that did demonstrate positive clinical effects were *Gymnema sylvestre* (GS). Of particular interest was the herb GS, because of its long history as a treatment for diabetes, and its range of unique and varied effects. In the Ayurvedic system of medicine, GS is referred to as “mesasrngi,” and both the dried leaf (mesasrngi leaf) and dried root (mesasrngi root) are used therapeutically.

### **Ayurvedic Concept**

According to the Ayurvedic Pharmacopoeia of India, both the dried leaf and root of GS, depending on dosage form and formulation, are also used in the treatment of svasa (bronchial asthma), kasa (cough), kustha (leprosy and other skin diseases), and vrana (wounds), among other conditions [9]. *G. sylvestre* (Asclepiadaceae) a vulnerable species is a slow growing, perennial, medicinal woody climber found in central and peninsular India. Its leaves, called “Gurmar” in India, are well known for their sweet taste suppressing activity and are used for the treatment of diabetes mellitus for over 2000 year, hence the name “Gurmar” meaning ‘sugar destroying’. It is used in food additives against obesity.

### **Plant perspective**

The plant belongs to Kingdom Plantae with Division Angiosperm and Class Dicotyledoneae. GS is native to south-Indian forests. It is a large tropical liana native to central and western India and can be also found in tropical Africa and in Australia [10-12]. The plant is documented to possess beneficial effects as digestive, anti-inflammatory, diuretic, hypoglycemic and anthelmintic. It is believed to be used in dyspepsia, constipation, jaundice, hemorrhoids, cardiomyopathy, asthma, bronchitis and leucoderma. A scrutiny of literature revealed some notable pharmacological activities of the plant such as antidiuretic, ant obesity, hypolipidemic, and antimicrobial, free radical scavenging and anti-inflammatory.

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**Photochemistry**

The major class of phytochemical belongs to *G. sylvestre* leaves contain triterpene saponins belonging to Oleanane and dammarene classes. Oleanane saponins are gymnemic acids and GS saponins, while dammarene saponins are gymnemasides. The other chemical constituents are flavones, anthroquinones, hentri-acontane, pentatriacontane, á and â-chlorophylls, phytin, resins, d-quercitol, tartaric acid, formic acid, butyric acid, lupeol, â-amylin related glycosides and stigma sterol, some alkaloids and anthroquinones [13,14]. Gymnemic acids have anti diabetic, ant sweetener and anti-inflammatory activities. Some of many phytochemicals found in *G. sylvestre* are and their pharmacological actions have been given in Table-1 [15].

Phytochemical	Pharmacological activity
Ascorbic-Acid	Acidulant, Aldose-Reductase-Inhibitor, Angiotensin-Receptor-Blocker, Anti AGE, AntiCrohn's, Antiaging, Antiatherosclerotic, Antidecubitic, Antidepressant, Antidote (Aluminum), Antidote (Paraquat), Antiedemic, Antigingivitic, Anti hepatotoxic, Antihistaminic, Antihypertensive, Antiinflammation, Anti-measles, Antimigraine, Antimutagenic, Antiobesity, Antiorchitic, Antioxidant, Antiparkinsonian, Antiseptic, Apoptotic, Beta-Adrenergic Receptor Blocker, Beta-Glucuronidase-Inhibitor, Collagenic, Fistula-Preventive, Hypotensive, Immunostimulant, Mucolytic, Urinary-Acidulant, Vulnerary
Beta-Carotene	AntiPMS, Antiacne, Antiaging, Antihyperkeratotic, Antilupus, Antimastitic, Antimutagenic, Antioxidant, Antiphotophobic, Antiporphyrin, Antiproliferant, Antistress, Antitumor, Antixerophthalmic, COX-1-Inhibitor, Colorant, Immunostimulant, Interferon-Synergist, Phagocytotic, Prooxidant, Thymoprotective
Betaine	Antigastritic, Antihomocystinuric, Ethanolytic, Hepatoprotective
Choline	Antialzheimeran, Antichoreic, Anticystinuric, Antidementia, Antidyskinetic, Antimanic, Cardio depressant, Cerebrotonic, Hepatoprotective, Hypotensive, Memorigenic
Conduritol-A	Aldose-Reductase-Inhibitor, Ant diabetic, Antihistaminic, Anti-inflammatory, Antipyretic, Antiseptic, Antitesticular, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypoglycemic, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Ribosome-Inactivator, Sedative, Serotonergic, Thyrotropic
Gymnemic-Acid	Antiflu, Antihistaminic, Antiinflammation, Antiobesity, Antipyretic, Antiseptic, Antiviral, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Sedative, Serotonergic, Thyrotropic
Gymnemic-Acid-B	Antiflu, Antihistaminic, Antiinflammation, Antiobesity, Antipyretic, Antiseptic, Antiviral, Cyclooxygenase-Inhibitor, Fungicide, Gastrostimulant, Hypotensive, Hypothermic, Immunostimulant, Molluscicide, Mutagenic, Nematicide, Progesteronigenic, Sedative, Serotonergic, Thyrotropic
Niacin	AntiMeniere's, Anti acrodynic, Antiallergic, Anti amblyopic, Antianginal, Antichilblain, Anticonvulsant, Antihistaminic, Antiinsomnic, Antineuralgic, Antiparkinsonian, Antipellagic, Antiscotomic, Hepatoprotective, Sedative, Serotonergic

**Table 1:** Phytochemicals found in *G. sylvestre* [15].

**Medicinal usage**

The anti diabetic array of molecules has been identified as a group of closely related gymnemic acids. After examination of the results of several investigations it is found that *G. sylvestre* leaves have been found to cause hypoglycemia in laboratory animals to treat onset of diabetes mellitus (NIDDM). When GS leaf extract is administered to a diabetic patient, there is stimulation of the pancreas which results in increased insulin secretion. These compounds have also been found to increase fecal excretion of cholesterol. Other uses for GS leaf extract are its ability to act as a laxative, diuretic, and cough suppressant [16-18]. These other actions would be considered adverse reactions when GS is used for its glucose lowering effect in diabetes. GS leaf extract, notably the peptide 'Gurmarin', has been found to interfere with the ability of the taste buds on the tongue to taste sweet and bitter. Gymnemic acid has a similar effect. It is believed that by inhibiting the sweet taste sensation, it will limit their intake of sweet foods, and this activity may be partially responsible for its hypoglycemic effect. There are some possible mechanisms by which gymnemic acids exert its hypoglycemic effects by several ways like, it increases secretion of insulin, promotes regeneration of islet cells, increases utilization of glucose: it is shown to increase the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase, and it causes inhibition of glucose absorption from intestine by binding the glucose binding sites on transport receptors [19].

**Mechanism of Action of Gymnemic Acids**

The main constituent of GS is believed to be gymnemic acid, a mixture of at least 17 different saponins. Gymnemic acid formulations have been found useful against obesity, according to recent reports. This is attributed to the ability of gymnemic acids to delay the glucose absorption in the blood. The atomic arrangement of gymnemic acid molecules is similar to that of glucose molecules. These molecules fill the receptor locations on the taste buds thereby preventing its activation by sugar molecules present in the food, thereby curbing the sugar craving. Similarly, gymnemic acid molecules fill the receptor location in the absorptive external layers of the intestine thereby preventing the sugar molecules absorption by the intestine, which results in low blood sugar level. There are some possible mechanisms by which the leaves and especially gymnemic acids from GS exert its hypoglycemic effects are:

- It increases secretion of insulin
- It promotes regeneration of islet cells
- It increases utilization of glucose: It is shown to increase the activities of enzymes responsible for utilization of glucose by insulin-dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase and
- It causes inhibition of glucose absorption from intestine, the exact action being unknown. It could be involve one or more mechanisms [13,20].

**Drug Dosage and Administration**

Clinical studies investigating ant diabetic effects have typically used 200 or 400mg GS leaves extract daily standardized to contain 25% gymnemic acids. The patients showed a significant reduction in blood glucose, glycosylated hemoglobin and glycosylated plasma proteins, and conventional drug dosage could be decreased. 22% diabetic patients were able to discontinue their conventional drug and maintain their blood glucose homeostasis with drug alone. These data suggest that the beta cells may be regenerated and/or repaired in Type 2 diabetic patients on GS leaf extract supplementation. This is supported by the appearance of raised serum insulin levels too [21].

**Drug Interaction and Side-effects**

As such no obvious drug interaction is documented in literature but caution has been made for the drugs responsible for lowering blood glucose levels. If this is used with anti-diabetic drugs, hypoglycemia may occur probably due to synergistic action. No safety data is available for its use in pregnancy, therefore, it is not advisable in pregnant and lactating mothers.

### GS in obesity

Obesity and its effect on human body Obesity and associated type 2 diabetes mellitus are the emerging epidemic of this new century. It is characterized by the increased storage of triglycerides (fat molecules) in adipose tissue thereby causing insulin resistance. It could also be defined as the condition of a human being in which the body contains more fat than required and which can lead to a disease state.

### Conclusion

In recent years, ethno botanical and traditional uses of natural compounds, especially of plant origin received much attention as they are well tested for their efficacy and generally believed to be safe for human use. They obviously deserve scrutiny on modern scientific lines such as physiochemical characterization, biological evaluation, toxicity studies, investigation of molecular mechanism of action(s) of isolated phyto principle and their clinical trials. These are necessary classical approaches in search of new lead molecule for management of various diseases. Diabetes is now becoming a common disease through the world and a lot of new drugs are being synthesized for the same. GS Leaves has been used by natural clinics in India for centuries to support healthy blood sugar levels. The taste of GS suppresses the ability to detect sweet tastes. It has an important place among such antidiabetic medicinal herbs. It has shown experimental or clinical anti-diabetic activity and it boosts our insulin level. Since each part of GS has some medicinal property, it is very much commercially exploitable.

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**Conflict of Interest:** None

### Side Effects & Safety

Gymnema is POSSIBLY SAFE when taken by mouth appropriately for up to 20 months.

### Special Precautions & Warnings:

**Pregnancy and breast-feeding:** There is not enough reliable information about the safety of taking gymnema if you are pregnant or breast feeding. Stay on the safe side and avoid use.

**Diabetes:** Gymnema can lower blood sugar levels in people with diabetes. Watch for signs of low blood sugar (hypoglycemia) and monitor your blood sugar carefully if you have diabetes and use gymnema.

**Surgery:** Gymnema might affect blood sugar levels and could interfere with blood sugar control during and after surgical procedures. Stop using gymnema at least 2 weeks before a scheduled surgery.

### Moderate Interaction

Be cautious with this combination

- **Insulin interacts with GYMNEMA**

Gymnema might decrease blood sugar. Insulin is also used to decrease blood sugar. Taking gymnema along with insulin might cause your blood sugar to be too low. Monitor your blood sugar closely. The dose of your insulin might need to be changed.

- **Medications for diabetes (Antidiabetes drugs) interacts with GYMNEMA**

Gymnema supplements seem to lower blood sugar in people with diabetes. Diabetes medications are also used to lower blood sugar. Taking gymnema along with diabetes medications might cause your blood sugar to go too low. Monitor your blood sugar closely. The dose of your diabetes medication might need to be changed. Some medications used for diabetes include glimepiride (Amaryl), glyburide (DiaBeta, Glynase PresTab, Micronase), insulin, pioglitazone (Actos), rosiglitazone (Avandia), chlorpropamide (Diabinese), glipizide (Glucotrol), tolbutamide (Orinase), and others.

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